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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,727	04/02/2004	John D. Brennan	571-933	9476

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EXAMINER	
JUNG, UNSU	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/815,727	BRENNAN ET AL.	
	Examiner	Art Unit	
	Unsu Jung	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' amendments to cancel claim 2 and amend claims 1, 3, 5, and 10-12 in the reply filed on November 14, 2005 have been acknowledged and entered.

2. Applicants' amendments to the drawings in the reply filed on December 14, 2005 have been acknowledged and entered.

3. Claims 1 and 3-25 are pending.

Drawings

4. The drawings were received on December 14, 2005. These drawings are acceptable.

Objections Withdrawn

5. Applicants' arguments, see p7, filed November 14, 2005, with respect to the claim objections have been fully considered and are persuasive. The objection of claims 5 and 15 in the Office Action filed on July 13, 2005 has been withdrawn.

A typo is noted in line 8 on p9 of Applicants' reply filed on November 14, 2005 as Applicants request that objections to claims 3 and 15 be withdrawn. The

objection of claims 5 and 15 is withdrawn as no objection was made to claim 3 in the Office Action filed on July 13, 2005.

Rejections Withdrawn

6. Applicant's arguments, see p7, filed November 14, 2005, with respect to the rejection under 35 U.S.C. 112, second paragraph have been fully considered and are persuasive. The rejection of claims 10-13 and 25 under 35 U.S.C. 112, second paragraph in the Office Action filed on July 13, 2005 has been withdrawn.

7. Applicant's arguments, see p, filed 10, with respect to the rejection under 35 U.S.C. 102(b) as being anticipated by Stowell et al. (U.S. Patent No. 6,284,163, Sep. 4, 2001) have been fully considered and are persuasive. The rejection of claims 1, 7, 91 and 11 under 35 U.S.C. 102(b) as being anticipated by Stowell et al. in the Office Action filed on July 13, 2005 has been withdrawn in light of amendment of claim 1.

8. Applicant's arguments, see p13, filed on November 14, 2005, with respect to the rejection under 35 U.S.C. 103(a) as being unpatentable over Besanger et al. (*J. Phys. Chem. B*, Published on Web Sept. 20, 2002, Vol. 106, pp10535-10542) in view of Stowell et al. (U.S. Patent No. 6,284,163, Sep. 4, 2001) have been fully considered and are persuasive. The rejection of claim 8 under 35 U.S.C. 103(a) as being unpatentable over Besanger et al. in view of Stowell et al. in the Office Action filed on July 13, 2005 has been withdrawn.

9. Applicant's arguments, see p13, filed November 14, 2005, with respect to the rejection under 35 U.S.C. 103(a) as being unpatentable over Stowell et al. (U.S. Patent No. 6,284,163, Sep. 4, 2001) in view of Dattagupta et al. (Patent No. 5,711,964, Jan. 27, 1998) have been fully considered and are persuasive. The rejection of claim 10 under 35 U.S.C. 103(a) as being unpatentable over Stowell et al. in view of Dattagupta et al. in the Office Action filed on July 13, 2005 has been withdrawn.

10. Applicant's arguments, see p13, filed November 14, 2005, with respect to the rejection under 35 U.S.C. 103(a) as being unpatentable over Besanger et al. (*J. Phys. Chem. B*, Published on Web Sept. 20, 2002, Vol. 106, pp10535-10542) in view of Dattagupta et al. (Patent No. 5,711,964, Jan. 27, 1998) have been fully considered and are persuasive. The rejection of claim 10 under 35 U.S.C. 103(a) as being unpatentable over Besanger et al. in view of Dattagupta et al. in the Office Action filed on July 13, 2005 has been withdrawn.

11. Applicant's arguments, see p14, filed November 14, 2005, with respect to the rejection under 35 U.S.C. 103(a) as being unpatentable over Stowell et al. (U.S. Patent No. 6,284,163, Sep. 4, 2001) in view Lapidot et al. (U.S. PG Pub. No. US 2002/0064541 A1, Filed Oct April 21, 2000) and Smith et al. (*J. Am. Chem. Soc.*, Published on Web Mar. 28, 2002, Vol. 124, pp4247-4252) have been fully considered and are persuasive. The rejection of claims 12 and 13

under 35 U.S.C. 103(a) as being unpatentable over Stowell et al. in view Lapidot et al. and Smith et al. in the Office Action filed on July 13, 2005 has been withdrawn.

12. Applicant's arguments, see p, filed 16, with respect to the rejection under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 16, 37, 38, 39, 41, 42, 47, 49, and 51 of copending Application No. 10/647,174 have been fully considered and are persuasive. The rejection of claims 1-25 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 16, 37, 38, 39, 41, 42, 47, 49, and 51 of copending Application No. 10/647,174 in view of Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421) in the Office Action filed on July 13, 2005 has been withdrawn in light of abandoned Application No. 10/647,174.

Response to Amendment

13. The Declaration under 37 CFR 1.132 filed on November 14, 2005 is sufficient to overcome the rejection of claims 1-6, 9, and 14 based upon 35 U.S.C. 102(a) as being anticipated by Besanger et al. (*J. Phys. Chem. B*, Published on Web Sept. 20, 2002, Vol. 106, pp10535-10542) in the Office Action filed on July 13, 2005.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

15. Claims 1-4, 11 and 14-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421).

Gill anticipates instant claims by teaching a method of immobilizing membrane-associated molecules in silica matrixes comprising combining a liposome-assembly, which includes the membrane associated molecule (p3405, *General Considerations for the Encapsulation of Biomolecular Structures*), with a protein- and membrane-compatible sol-gel precursor under conditions to allow a gel to form (pp3404, Abstract), wherein the protein- and membrane-compatible sol-gel precursor is an organic polyol silane (alkoxy-silanes mixed with an organic polyol such as glycerol, pp3406-8, *The Essentials of Sol-Gel Nano-bioencapsulation* and p3407, Figure 1).

With respect to claim 11, Gill teaches a method comprising the steps of:

(i) combining an aqueous solution of the protein and membrane-compatible, sol gel precursor with an aqueous solution of a liposome assembly comprising the membrane-associated molecule;

(ii) adjusting the pH of the combination of (i) so that it is in the range of about 4-11.5;

(iii) shaping the combination into a desired shape;

(iv) allowing the combination to gel;

(v) aging and partially drying the gel.

With respect to claim 14, Gill teaches a method of immobilizing membrane-associated molecules in silica matrixes, wherein the membrane-associated molecule and the protein and membrane-compatible, sol-gel precursor are combined in the presence of an indicator molecule and/or in the presence of one or more ligands for the membrane-associated molecule (p3415, column 1, lines 1-5).

With respect to claims 15-19, Gill teaches a method of immobilizing membrane-associated molecules in silica matrixes further comprising combining the liposome assembly and sol-gel precursor in the presence of one or more additives such as polyethylene glycol (p3407, Figure 1).

16. Claims 1, 11, and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Robotti (U.S. PG Pub. No. 2003/0148291 A1, Filed Feb. 5, 2002).

Robotti anticipates instant claims by teaching a method of immobilizing membrane-associated molecules in silica matrixes comprising combining a liposome-assembly, which includes the membrane associated molecule (p3, paragraph [0034]), with a protein- and membrane-compatible sol-gel precursor under conditions to allow a gel to form (p5, paragraph [0054]), wherein the protein- and membrane-compatible sol-gel precursor is sodium silicate (p6, paragraph [0062]).

With respect to claim 11, Robotti teaches a method comprising the steps of (p5, paragraphs [0054] and [0059]):

(i) combining an aqueous solution of the protein and membrane-compatible, sol gel precursor with an aqueous solution of a liposome assembly comprising the membrane-associated molecule;

(ii) adjusting the pH of the combination of (i) so that it is in the range of about 4-11.5;

(iii) shaping the combination into a desired shape;

(iv) allowing the combination to gel;

(v) aging and partially drying the gel.

With respect to claim 14, Robotti teaches a method of immobilizing membrane-associated molecules in silica matrixes, wherein the membrane-associated molecule and the protein and membrane-compatible, sol-gel precursor are combined in the presence of an indicator molecule and/or in the presence of one or more ligands for the membrane-associated molecule (column 10, paragraphs [0099]-[0102]).

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.**

18. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

19. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of

35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claims 5, 6, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421) in view of Montgomery (U.S. Patent No. 6,093,302, July 25, 2000).

Gill teaches a method of immobilizing membrane-associated molecules in silica matrixes as discussed above, wherein the organic polyol silane precursor is poly(glyceryl silicate). However, Gill fails to teach a method, wherein the organic polyol silane precursor is diglycerylsilane.

Montgomery teaches a well known polymerization method in the art, wherein the number of monomers can be varied from a number two or greater (column 16, lines 45-63).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was made to include in the method of Gill with a method of varying monomer number to be two as taught by Montgomery in order to obtain di(glyceryl silicate) as it would take only a routine skill to vary the number of monomers during a polymerization process.

With respect to claim 8, Gill discloses the claimed invention, a method of immobilizing membrane-associated molecule such as bacteriorhodopsin in silica matrix (p3415, Table 4). However, Gill teaches a method of encapsulation of bacteriorhodopsin using trimethoxysilane (TMOS), which is not an organic polyol

silane precursor. Gill further teaches that entrapped photoactive proteins such as bacteriorhodopsin can be used in solid state optical devices and transducers (p3415, right column, lines 4-6). Although Gill fails to specifically teach a method to encapsulate bacteriorhodopsin with an organic polyol silane, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of immobilizing membrane-associated molecule using organic polyol silane precursor as taught by Gill with a bacteriorhodopsin as a membrane-associated molecule in order to use the photoactive protein such as bacteriorhodopsin as an optical device and transducer.

21. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421).

Gill teaches a method of immobilizing membrane-associated molecules in silica matrixes as discussed above, wherein the organic polyol silane precursor is poly(glyceryl silicate). Gill teaches that entrapped photoactive proteins such as bacteriorhodopsin can be used in solid state optical devices and transducers (p3415, right column, lines 4-6). Gill further discloses a method of immobilizing membrane-associated molecule such as bacteriorhodopsin in silica matrix (p3415, Table 4). However, Gill teaches a method of encapsulation of bacteriorhodopsin using trimethoxysilane (TMOS), which is not an organic polyol silane precursor. Although Gill fails to specifically teach a method to encapsulate bacteriorhodopsin with an organic polyol silane, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method

of immobilizing membrane-associated molecule using organic polyol silane precursor as taught by Gill with a bacteriorhodopsin as a membrane-associated molecule in order to use the photoactive protein such as bacteriorhodopsin as an optical device and transducer.

22. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421) in view of Stowell et al. (U.S. Patent No. 6,284,163, Sep. 4, 2001).

Gill teaches a method of immobilizing membrane-associated molecules in silica matrixes as discussed above. However, Gill fails to teach a method, wherein the liposome comprises phospholipids.

Stowell et al. teaches a method of immobilizing membrane-associated molecules in silica matrixes comprising combining a liposome-assembly, which includes the membrane associated molecule (column 3, lines 59-64), with a protein- and membrane-compatible sol-gel precursor under conditions to allow a gel to form (column 3, lines 18-30). Lipid membranes and vesicles (liposomes) mimic the biological cell structure (column 1, lines 25-26). Due to its self-assembled uniform structure and resultant physicochemical properties, they have gained more research attention and application in a variety of fields (column 1, lines 26-28). However, lipid membranes and vesicles are fragile metastable systems (column 1, lines 28-29). The compositions of Stowell et al. are expected to have enhanced thermal and mechanical stability compared to conventional phospholipid vesicles and phospholipid lipid bilayer membranes (column 2, lines

49-52). Moreover, these compositions find application in ion specific filtration and desalination, and as detections biosensors, biocatalysts, high performance materials, optical, and diagnostic devices.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Gill with a liposome-assembly, which includes the membrane associated molecule, wherein liposome comprises phospholipids as taught by Stowell et al. in order to provide more thermally and mechanically stable liposome-assembly, which includes a membrane associated molecule, for application in ion specific filtration and desalination, and as detections biosensors, biocatalysts, high performance materials, optical and diagnostic devices.

23. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Robotti (U.S. PG Pub. No. 2003/0148291 A1, Filed Feb. 5, 2002) in view of Stowell et al. (U.S. Patent No. 6,284,163, Sep. 4, 2001).

Robotti teaches a method of immobilizing membrane-associated molecules in silica matrixes as discussed above. However, Gill fails to teach a method, wherein the liposome comprises phospholipids.

Stowell et al. teaches a method of immobilizing membrane-associated molecules in silica matrixes comprising combining a liposome-assembly, which includes the membrane associated molecule (column 3, lines 59-64), with a protein- and membrane-compatible sol-gel precursor under conditions to allow a gel to form (column 3, lines 18-30). Lipid membranes and vesicles (liposomes)

mimic the biological cell structure (column 1, lines 25-26). Due to its self-assembled uniform structure and resultant physicochemical properties, they have gained more research attention and application in a variety of fields (column 1, lines 26-28). However, lipid membranes and vesicles are fragile metastable systems (column 1, lines 28-29). The compositions of Stowell et al. are expected to have enhanced thermal and mechanical stability compared to conventional phospholipid vesicles and phospholipid lipid bilayer membranes (column 2, lines 49-52). Moreover, these compositions find application in ion specific filtration and desalination, and as detections biosensors, biocatalysts, high performance materials, optical, and diagnostic devices.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Robotti with a liposome-assembly, which includes the membrane associated molecule, wherein liposome comprises phospholipids as taught by Stowell et al. in order to provide more thermally and mechanically stable liposome-assembly, which includes a membrane associated molecule, for application in ion specific filtration and desalination, and as detections biosensors, biocatalysts, high performance materials, optical and diagnostic devices.

24. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421) in view of Stowell et al. (U.S. Patent No. 6,284,163, Sep. 4, 2001) as applied to

claim 9 above, and further in view of Dattagupta et al. (Patent No. 5,711,964, Jan. 27, 1998).

Gill in view of Stowell et al. teaches a method of immobilizing membrane-associated molecules in silica matrixes as discussed above. However, Gill in view of Stowell et al. fails to teach the use of lipid comprising 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC) in liposome assembly.

Dattagupta et al. teaches that an amphiphile such as DOPC (column 6, line 26 and column 12, lines 33-38) is used to form a liposomal vesicle (column 6, lines 45-46).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Gill in view of Stowell et al. with an amphiphilic DOPC as taught by Dattagupta et al. in order to construct liposomal vesicles.

25. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Robotti (U.S. PG Pub. No. 2003/0148291 A1, Filed Feb. 5, 2002) in view of Stowell et al. (U.S. Patent No. 6,284,163, Sep. 4, 2001) as applied to claim 9 above, and further in view of Dattagupta et al. (Patent No. 5,711,964, Jan. 27, 1998).

Robotti in view of Stowell et al. teaches a method of immobilizing membrane-associated molecules in silica matrixes as discussed above. However, Robotti in view of Stowell et al. fails to teach the use of lipid comprising 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC) in liposome assembly.

Dattagupta et al. teaches that an amphiphile such as DOPC (column 6, line 26 and column 12, lines 33-38) is used to form a liposomal vesicle (column 6, lines 45-46).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Robotti in view of Stowell et al. with an amphiphilic DOPC as taught by Dattagupta et al. in order to construct liposomal vesicles.

26. Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421) in view Lapidot et al. (U.S. PG Pub. No. US 2002/0064541 A1, Filed Oct April 21, 2000) and Smith et al. (*J. Am. Chem. Soc.*, Published on Web Mar. 28, 2002, Vol. 124, pp4247-4252).

Gill teaches a method of immobilizing membrane-associated molecules in silica matrixes as discussed above. However, Gill fails to teach the use of aqueous buffer, comprising about 5% to about 50% (v/v) of glycerol.

Lapidot et al. teaches that the disintegration of microcapsules prepared by sol-gel process is effected by drying (p9, paragraph [0154]). The drying of the microcapsules is effected by the evaporation of water, which leaves the microcapsules exposed to the environment and thus triggers their disintegration (p9, paragraph [0155]). Additives that are capable of maintaining humidity and moisture can be added during the sol-gel process to control the surface nature of

the sol-gel matrix (p9, paragraph [0156]). Examples of humectants include glycerol (p10, paragraph [0174]).

Smith et al. teaches a method of encapsulating an enzyme using a sol-gel technique (Abstract). During a gelation process, phosphate buffer comprising 10% glycerol was used during the wash step in order to remove the ethanol produced in the gelation reaction and during the aging and drying steps (p4249, left column, *Casting of Sol-Gel Monoliths*).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Gill with a use of humectant such as glycerol in a buffer solution as taught by Smith et al. to use during the drying process as taught by Lapidot et al. in order to control the surface nature of the sol-gel matrix.

27. Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robotti (U.S. PG Pub. No. 2003/0148291 A1, Filed Feb. 5, 2002) in view Lapidot et al. (U.S. PG Pub. No. US 2002/0064541 A1, Filed Oct April 21, 2000) and Smith et al. (*J. Am. Chem. Soc.*, Published on Web Mar. 28, 2002, Vol. 124, pp4247-4252).

Robotti teaches a method of immobilizing membrane-associated molecules in silica matrixes as discussed above. However, Gill fails to teach the use of aqueous buffer, comprising about 5% to about 50% (v/v) of glycerol.

Lapidot et al. teaches that the disintegration of microcapsules prepared by sol-gel process is effected by drying (p9, paragraph [0154]). The drying of the

microcapsules is effected by the evaporation of water, which leaves the microcapsules exposed to the environment and thus triggers their disintegration (p9, paragraph [0155]). Additives that are capable of maintaining humidity and moisture can be added during the sol-gel process to control the surface nature of the sol-gel matrix (p9, paragraph [0156]). Examples of humectants include glycerol (p10, paragraph [0174]).

Smith et al. teaches a method of encapsulating an enzyme using a sol-gel technique (Abstract). During a gelation process, phosphate buffer comprising 10% glycerol was used during the wash step in order to remove the ethanol produced in the gelation reaction and during the aging and drying steps (p4249, left column, *Casting of Sol-Gel Monoliths*).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Robotti with a use of humectant such as glycerol in a buffer solution as taught by Smith et al. to use during the drying process as taught by Lapidot et al. in order to control the surface nature of the sol-gel matrix.

28. Claims 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421) in view Keeling-Tucker et al. (*Chem. Mater.*, Published on Web July 31, 2001, Vol. 13, pp3331-3350).

Gill teaches a method of immobilizing membrane-associated molecules in silica matrixes as discussed above. However, Gill fails to teach the use of polyethelene oxide (PEO), PEO-NH2, and poly NIPAM.

Keeling-Tucker et al. teaches a method of incorporating hydrophilic polymers within silicate materials with the silica sol (p3339, Hydrophilic Polymers, column 1, lines 1-5). The development of Class I materials generally involves the dispersion of hydrophobic, hydrophilic, or charged polymers or surfactants into sol-gel precursor materials during the hydrolysis step (p3338, *B. Materials with Dispersed Organic Additives (Class I Materials),* column 2, lines 2-6). Such materials can either interact with silica, thus modifying the properties of the solvent-silica interface, or can segregate into independent phases, resulting in unique structures such as interpenetrating polymer networks (p3338, *B. Materials with Dispersed Organic Additives (Class I Materials),* column 2, lines 6-11). The additive, PEO, was able to organize by hydrophobic interactions to provide a relatively large volume fraction of the organic subphase (p3340, column 2, paragraph 4, line 11-p3341, column 1, paragraph 1, line 1).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Gill with the use of an additive, PEO, in order to provide segregation into independent phases prior to gelation.

29. Claims 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421) in view of Leung et al. (Patent No. 6,204,202, Filed Apr. 14, 1999).

Gill teaches a method of immobilizing membrane-associated molecules in silica matrixes as discussed above. However, Gill fails to teach the use of polyethylene oxide (PEO), PEO-NH2, and poly NIPAM.

Leung et al. teaches a method for making silica nanoporous films (such as sol-gel) of sufficient mechanical strength that are also optimized to have a desirably low and stable dielectric constant, without the need for further processing to make the film hydrophobic (column 3, lines 19-26) by mixing a non-volatile thermally degradable polymer with an organic and/or inorganic silicon-based material (column2, lines 44-58 and column 3, lines 34-36). A useful nanoporous material must meet a number of criteria, including having a dielectric constant falling within the required value range, having a suitable thickness, having an ability of effectively fill gaps, and having an effective degree of hydrophobicity (column 2, lines 60-66). If the material is not strong enough, despite achieving the other requirements, the pore structure may collapse, resulting in high material density, and therefore an undesirably high dielectric constant.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Gill with an additive (thermally degrading polymer such as PEO having a molecular weight ranging

from about 200 to 2,000,000 Daltons, column 4, lines 16-22) as taught by Leung et al. in order to make silica nanoporous films (such as sol-gel) of sufficient mechanical strength that are also optimized to have a desirably low and stable dielectric constant, without the need for further processing to make the film hydrophobic.

30. Claims 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421) in view Delamarche et al. (*Langmuir*, Published on Web Sept. 11, 2003, Vol. 19, 8749-8758).

Gill teaches a method of immobilizing membrane-associated molecules in silica matrixes as discussed above. However, Gill fails to teach the use of an additive selected from compounds of Formula 5.

Delamarche et al. teaches the use of PEO silane onto a sol-gel polymer, poly(dimethylsiloxane) ink, resulting in a stable hydrophilic structure (p8755, 3. Conclusion, column 2, lines 1-6). The method of using PEO silane is simple and particularly effective when proteins are active molecules (p8755, 3. Conclusion, column 2, line 4-p8756, column 1, line 1).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Gill with an additive of Formula 5 (p8751, Scheme 1, Formula 17) as taught by Delamarche et al. in order to provide a simple and effective means to construct a stable hydrophilic structure.

Claims 16, 24 and 25 are not supported by the disclosure in parent application (10/712,015). Therefore, the priority date of the parent application is not applicable for the claims 16, 24, and 25 and the above reference, Delamarche et al. meets the criteria for a prior art.

Double Patenting

31. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

32. Claims 1 and 3-25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 16, 37, 38, 39, 41, 42, 47, 49, and 51 of copending Application No. 10/814,123 in view of Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421).

Copending Application No. 10/814,123 teaches a method of preparing siliceous materials comprising combining a sol-gel precursor (organic polyol

silane), a biomolecule of interest and one or more additives under conditions which allow a gel to form. However, copending Application No. 10/814,123 fails to teach a method incorporating a membrane-associated molecule.

Gill teaches method of encapsulation of proteins, which are part of assemblies such as bilayers, vesicles, and membranes in order to preserve the gross structural integrity and large-scale internal mobilities of these structures (p3406, left column, 5th paragraph).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of the copending Application No. 10/647,174, a step of incorporating membrane associated molecules into bilayers, vesicles, or membranes as taught by Gill in order to preserve the gross structural integrity and large-scale internal mobilities of these structures.

This is a provisional obviousness-type double patenting rejection.

33. Claims 1 and 3-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-27 of copending Application No. 10/712,015. Although the conflicting claims are not identical, they are not patentably distinct from each other because each teach a method of immobilizing membrane-associated molecules in silica matrixes comprising combining a liposome-assembly, which includes the membrane associated molecule, with a protein- and membrane-compatible sol-gel precursor under conditions to allow a gel to form, wherein the protein- and membrane-compatible sol-gel precursor is sodium silicate and it would be obvious to one of

ordinary skill in the art that the claims of copending Application would encompass the claims of current application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

34. Applicant's arguments filed on November 14, 2005 have been fully considered but they are not persuasive.

35. Applicants argue that there is not specific teaching of a membrane-associated molecule in combination with an organic polyol silane precursor in Figure 1 of Gill, which refers to "biomolecule" as the species for entrapment (p11). Applicants further contend that there is no specific reference to membrane-associated biomolecules. This argument is not found persuasive as Gill does teach membrane proteins (p3405, right column, lines 52-61) and cell membrane fractions, which would contain membrane proteins (p3405, left column, lines 59-63), as biomolecules.

Applicants further submit that Figure 1 does not specifically describe combining organic polyol silanes with any biomolecule and Figure 1 refers to the combination of alkoxy silanes with glycerol in a transesterification reaction followed by partial hydrolysis, which produces poly(glyceryl silicate), which is partially hydrolyzed and polycondensed precursor. This argument is not found

persuasive because poly(glyceryl silicate) is an organic polyol silane and is not a polycondensed precursor.

Since the prior art fulfills all the limitations currently recited in the claims, the invention as currently recited would read upon the prior art.

36. Applicant's arguments with respect to claim 7 have been considered but are moot in view of the new ground(s) of rejection.

37. With respect to the rejection of claims 12 and 13 under 35 U.S.C. 103(a) as being obvious over Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421) in view Lapidot et al. (U.S. PG Pub. No. US 2002/0064541 A1, Filed Oct April 21, 2000) and Smith et al. (J. Am. Chem. Soc., Published on Web Mar. 28, 2002), Applicants argue that Lapidot et al. and Smith et al. do not teach or remotely suggest the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes or sodium silicate. This argument is not found persuasive as the method of the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes is taught by Gill as discussed above. Lapidot et al. teaches that additives (humectants such as glycerol), which are capable of maintaining humidity and moisture, can be added during the sol-gel process to control the surface nature of the sol-gel matrix and Smith et al. teaches a method of encapsulating an enzyme using a sol-gel technique, during which phosphate buffer comprising 10% glycerol was used during the wash step in order to

remove the ethanol produced in the gelation reaction and during the aging and drying steps as discussed above.

38. With respect to the rejection of claims 20 and 21 under 35 U.S.C. 103(a) as being obvious over Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421) in view Keeling-Tucker et al. (*Chem. Mater.*, Published on Web July 31, 2001, Vol. 13, pp3331-3350), Applicants argue that Keeling-Tucker et al. do not teach or remotely suggest the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes or sodium silicate. This argument is not found persuasive as the method of the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes is taught by Gill as discussed above. Keeling-Tucker et al. teaches a use of an additive, PEO, during a sol-gel process in order to provide segregation into independent phases prior to gelation as discussed above.

39. With respect to the rejection of claims 20-23 under 35 U.S.C. 103(a) as being obvious over Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421) in view of Leung et al. (Patent No. 6,204,202, Filed Apr. 14, 1999), Applicants argue that Leung et al. do not teach or remotely suggest the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes or sodium silicate. This argument is not found persuasive as the method of the encapsulation of membrane-associated

molecules in sol-gel materials prepared from polyol-modified silanes is taught by Gill as discussed above. Leung et al. teaches a use of an additive, thermally degrading polymer such as PEO having a molecular weight ranging from about 200 to 2,000,000 Daltons, in order to make silica nanoporous films (such as sol-gel) of sufficient mechanical strength that are also optimized to have a desirably low and stable dielectric constant, without the need for further processing to make the film hydrophobic as discussed above.

40. With respect to the rejection of claims 24 and 25 under 35 U.S.C. 103(a) as being obvious over Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421) in view Delamarche et al. (*Langmuir*, Published on Web Sept. 11, 2003, Vol. 19, 8749-8758), Applicants argue that Delamarche et al. do not teach or remotely suggest the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes or sodium silicate. This argument is not found persuasive as the method of the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes is taught by Gill as discussed above. Delamarche et al. teaches a use of an additive of Formula 5 recited in claim 25 in a sol-gel process in order to provide a simple and effective means to construct a stable hydrophilic structure as discussed above.

41. With respect to the rejection of 1-25 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being

unpatentable over claims 1-9, 16, 37, 38, 39, 41, 42, 47, 49, and 51 of copending Application No. 10/814,123 in view of Gill (*Chem. Mater.*, Web Release Date of July 4, 2001, Vol. 13, pp3404-3421), Applicants argue that Gill do not teach or remotely suggest the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes or sodium silicate. This argument is not found persuasive as the method of the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes is taught by Gill as discussed above.

Conclusion

42. No claim is allowed.

43. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Unsu Jung whose telephone number is 571-272-8506. The examiner can normally be reached on M-F: 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through

Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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